

Response of atrial flutter to overdrive atrial pacing and intravenous disopyramide phosphate, singly and in combination

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SUMMARY Ten patients who suffered spontaneous paroxysms of atrial flutter were investigated by electrophysiological techniques. Two had overt Wolff-Parkinson-White syndrome; three Lown-Ganong-Levine syndrome; and one a concealed accessory atrioventricular connection. Atrial flutter was initiated, at study, by right atrial pacing and electrograms from the right atrium and coronary sinus were observed for at least five minutes to ensure stable flutter in both atria.

Atrial flutter was terminated by 2.5 s or 5 s bursts of atrial pacing at rates 10, 50, or 100 beats/min faster than the intrinsic flutter rate in only two patients. Atrial flutter, which was reinitiated in two patients, was then treated with intravenous disopyramide phosphate, 2 mg/kg body weight, infused over five minutes. In all 10 patients the atrial rate slowed from a mean of 310 ± 39 beats/min to 217 ± 27 beats/min and atrial flutter terminated in one case. Though the mean ventricular rate fell from 161 ± 52 beats/min to 156 ± 45 beats/min the atrioventricular conduction ratio fell from 2.17 ± 0.86 to 1.55 ± 0.59 and four patients were left with symptomatically significant increases of ventricular rate. In seven of nine patients overdrive atrial pacing, repeated after disopyramide, resulted in the conversion of atrial flutter to sinus rhythm.

In this study, overdrive atrial pacing and intravenous disopyramide, singly and in combination, terminated atrial flutter in nine of the 10 patients and it is suggested that this method may provide an effective alternative to direct current cardioversion.

In 1967, Haft and coworkers¹ reported the successful termination of atrial flutter by rapid atrial pacing. They also suggested that premedication with quinidine-like drugs potentiated the success of the technique. Though others²⁻¹¹ have used atrial pacing techniques to treat atrial flutter with variable and, at times, contradictory results^{12 13} little attention has been given to pretreatment with antiarrhythmic agents. Here we report the individual and combined results of overdrive atrial pacing and intravenous disopyramide phosphate in the treatment of paroxysms of atrial flutter.

Subjects and methods

Ten patients aged between 22 and 62 years were investigated for complaints of recurrent paroxysmal palpitations (Table 1). All patients had suffered documented attacks of atrial flutter and three patients also had attacks of "supraventricular"

tachycardia which were not thought to be atrial flutter. One patient presented with profound sinus bradycardia, sinus node arrest, and paroxysms of tachycardia. There was no clinical or radiographic evidence of organic heart disease though two patients were mildly hypertensive. The surface electrocardiogram was normal in four patients, showed sinus bradycardia in one, and a short PR interval in five. In two patients, the short PR interval was followed by broad QRS complexes of the Wolff-Parkinson-White pattern, type A. Routine blood tests, including thyroid function tests, were normal in all patients.

The patients underwent intracardiac electrophysiological investigation in the catheterisation laboratory or coronary care unit. All patients were studied in a fasting unsedated state and had not received medication for at least 72 hours before the study. Informed consent was obtained from each patient. Conventional electrophysiological investigations were performed as described elsewhere,¹⁴

but for the purpose of this study bipolar electrodes were positioned to record simultaneously or sequentially from the lateral wall of the right atrium (close to its junction with the superior vena cava) and the coronary sinus. Atrial flutter was initiated by rapid atrial pacing and the arrhythmia was observed for five minutes to ensure that there was stable flutter of both atria. At the end of this period, attempts were made to terminate atrial flutter by atrial pacing from the single right atrial site at a stimulus voltage of twice the diastolic threshold during sinus rhythm. Pacing rates were adjusted to 10, 50, and 100 beats/min faster than the spontaneous flutter rate and pacing was continued for periods of two and a half and five seconds. If this resulted in the successful termination of the arrhythmias, atrial flutter was restimulated and reobserved for a further five minutes to ensure stability. Disopyramide phosphate, at a dose of 2 mg/kg body weight, was then administered to all 10 patients. The infusion was given evenly over exactly five minutes, and continuous electrocardiographic recordings at a paper speed of 25 mm/s were made for a period of 10 minutes. Short strips were recorded at 100 mm/s at one minute intervals.

If atrial flutter had not terminated in response to disopyramide within 10 minutes of the start of the infusion, rapid atrial pacing for durations of two and a half and five seconds, at rates 10, 50, and 100 beats/min faster than the new flutter frequency, was again tried.

Atrial and ventricular rates were measured at one minute intervals throughout the study. Where the ventricular rate was irregular, the mean rate over a 10 second period was calculated. The atrioventricular conduction ratios were derived from these values. The maximum ventricular rate during the study period was noted. Results were analysed by the paired Student's *t* test.

Table 1 Clinical, electrocardiographic, and electrophysiological details of 10 patients with recurrent paroxysmal atrial flutter

Case no.	Age (y)	sex	Diagnosis	EPS
1	31	M	PAFI, SVT, LGL	PAFI, AVRT(CLAP)
2	44	M	PAFI	PAFI
3	39	F	PAFI, SAD, LGL	PAFI, SAD
4	62	M	PAFI, LGL	PAFI
5	22	F	PAFI	PAFI
6	58	M	PAFI	PAFI
7	48	M	PAFI	PAFI
8	62	M	PAFI, SVT, WPW	PAFI, AVRT(LAP)
9	48	M	PAFI, SVT, WPW	PAFI, AVRT(LAP)
10	52	M	PAFI	PAFI

PAFI, paroxysmal atrial flutter; SVT, supraventricular tachycardia; LGL, Lown-Ganong-Levine syndrome; SAD, sinuatrial disease; WPW, Wolff-Parkinson-White syndrome; AVRT, atrioventricular re-entrant tachycardia; CLAP, concealed left-sided accessory pathway; LAP, left-sided accessory pathway; EPS, electrophysiological study diagnosis.

Results

The results of routine electrophysiological studies in the 10 patients are summarised in Table 1. In six patients, no electrophysiological abnormality could be detected, but in one, abnormal sinus node function was documented and, in three, left-sided accessory atrioventricular pathways were disclosed and re-entrant tachycardias, using these pathways in the retrograde direction, were precipitated.

In all 10 patients, stable atrial flutter of both chambers was initiated by atrial pacing. The initial flutter frequency, the ventricular response rate, and the atrioventricular ratio are set out in Table 2, and illustrated in Fig. 1 and 2. The flutter rate varied between 230 beats/min and 375 beats/min (mean = 310 ± 39 beats/min), and in eight cases characteristic "saw tooth" flutter waves were seen, but, in two, both with overt Wolff-Parkinson-White syndrome, baseline oscillations were obscured

Table 2 Response of atrial flutter to disopyramide (diso) and overdrive atrial pacing (RAP)

Case no.	Atrial rate		Ventricular rate			A/V ratio		Termination		
	Pre	Post	Pre	Max	Post	Pre	Post	Diso	RAP (pre)	RAP (post)
1	320	220	130	171	130	2.46	1.69	0	0	+
2	353	230	86	110	90	4.10	2.55	+	0	NR
3	300	176	150	220	176	2.00	1.00	0	0	+
4	336	264	156	156	138	2.15	1.91	0	+	0
5	328	256	164	164	128	2.00	2.00	0	+	+
6	375	207	125	130	88	3.00	2.35	0	0	0
7	280	210	140	210	210	2.00	1.00	0	0	+
8	230	188	230	230	188	1.00	1.00	0	0	+
9	280	194	280	280	194	1.00	1.00	0	0	+
10	300	220	150	220	220	2.00	1.00	0	0	+
Mean	310	217	161	189	156	2.17	1.55			
SD (±)	39	27	52	49	45	0.86	0.59			

pre, pre-disopyramide; post, post-disopyramide; max, maximum ventricular rate observed during 10-minute observation period after the start of the disopyramide infusion; +, successful conversion; 0, unsuccessful conversion; NR, not relevant.

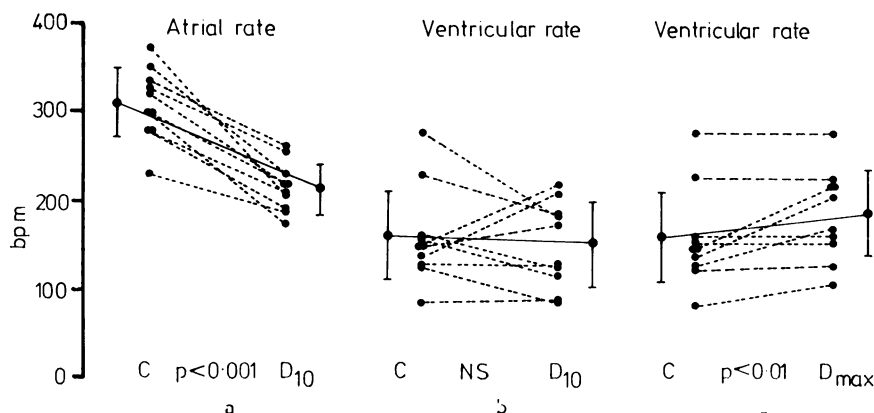


Fig. 1 Atrial and ventricular rates before and after disopyramide infusion. C, control; D₁₀, 10 minutes after disopyramide; D_{max}, maximum ventricular rate during the 10 minute observation period after the start of the disopyramide infusion; bpm, beats per minute.

by 1:1 conduction over the accessory pathway.

Rapid atrial pacing, before disopyramide (Fig. 3) successfully terminated two examples of atrial flutter (cases 4 and 5). In the remainder, flutter was entrained (six cases) or atrial capture was not achieved (two cases).

The infusion of disopyramide phosphate resulted in reduction of the atrial rate in all patients. The mean atrial rate fell significantly ($p < 0.001$) from 310 ± 39 beats/min to 217 ± 27 beats/min (Fig. 1a). In one patient atrial flutter terminated six minutes after the start of the disopyramide infusion. The ventricular rate response to disopyramide infusion was variable. Fig. 4 illustrates the response in case 9. Initially, the atrioventricular rate was 280 beats/min, and five minutes after the conclusion of the disopyramide infusion the 1:1 atrioventricular relation persisted at a rate of 194 beats/min. In case 7 (Fig. 5) 2:1 atrioventricular conduction was present initially but, in response to disopyramide, the atrial rate slowed from 270 beats/min to 200 beats/min with the development of 1:1 atrioventricular conduction. Results in the 10 patients are illustrated in Fig. 6 and are demonstrated graphically in Fig. 1b and 1c. In six patients, the ventricular rate increased at some time during the 10 minute observation period (Fig. 1c) and the mean increase (161 ± 52 to 189 ± 49 beats/min) was significant ($p < 0.01$). By the end of the observation period (Fig. 1b) there was an insignificant fall in the mean ventricular rate (161 ± 57 to 156 ± 45 beats/min), but the atrioventricular conduction ratio had significantly ($p < 0.01$) fallen (2.17 ± 0.86 to 1.55 ± 0.59).

In nine patients, the termination of the arrhythmia by overdrive atrial pacing was attempted again after the infusion of disopyramide. The technique proved

successful in seven cases, six of whom had not responded before disopyramide. In the two failures it was not possible to achieve atrial capture. In the successful cases, atrial pacing usually resulted in transient runs of atrial tachycardia or fibrillation before conversion to sinus rhythm. Atrial fibrillation of a duration longer than 5 s was not precipitated except in the two failures, who after completing the study were subjected to longer and faster periods of atrial pacing. One of these patients eventually required direct current cardioversion. The overall results of the combined technique are illustrated in Fig. 7.

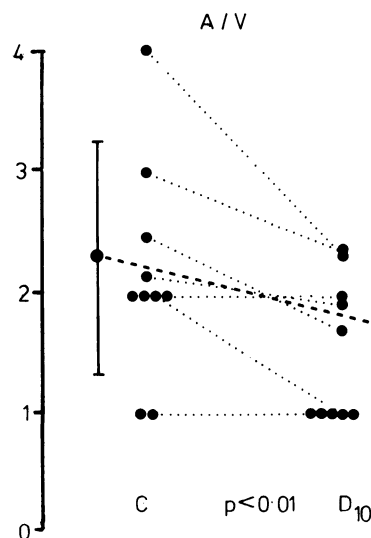


Fig. 2 The atrioventricular (A/V) ratio before (C) and after (D₁₀) disopyramide infusion.

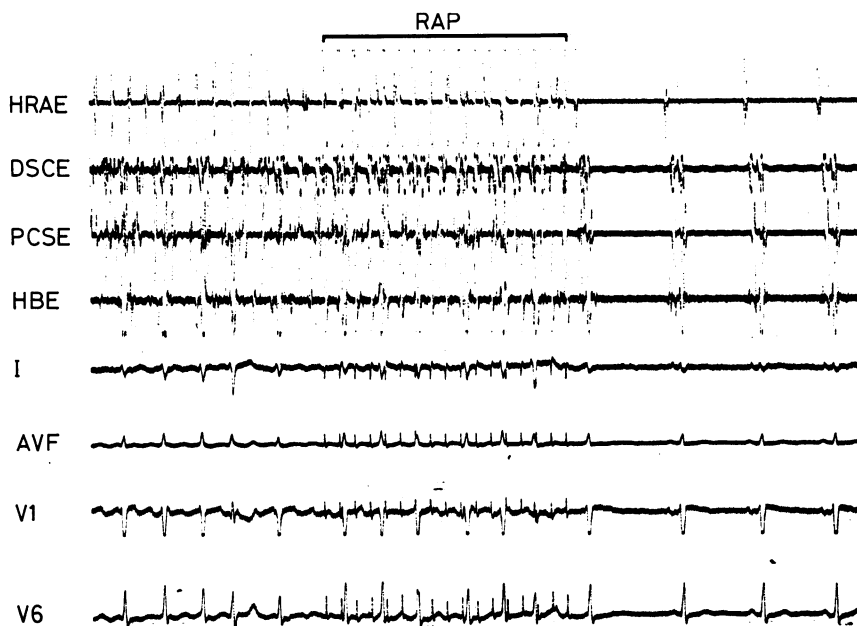


Fig. 3 The successful conversion of atrial flutter by rapid atrial pacing before the administration of disopyramide (case 4). The atrial flutter rate is 336 beats/min; the average ventricular rate is 156 beats/min; and the atrial pacing rate is 386 beats/min for 2.5 seconds.

HRAE, high right atrial electrogram; DCSE, distal coronary sinus electrogram; PCSE, proximal coronary sinus electrogram; HBE, His bundle region electrogram; RAP, rapid atrial pacing; I, aVF, V1, and V6 are surface electrocardiogram leads; paper speed, 25 mm/s.

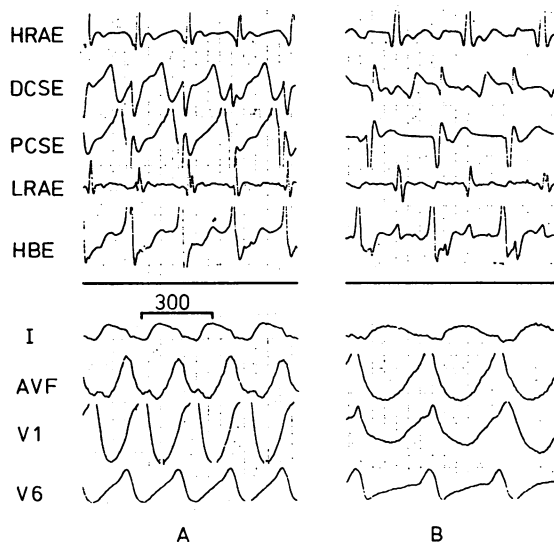


Fig. 4 Atrial flutter with 1:1 AV conduction via a left-sided accessory atrioventricular pathway before and 10 minutes after the infusion of disopyramide. The rate falls from 280 beats/min to 194 beats/min (case 9). LRAE, low right atrial electrogram. Paper speed, 100 mm/s.

Discussion

In 1963, Moe *et al.*¹⁵ showed that paced atrial extrastimulation could interrupt experimental reciprocating atrioventricular nodal tachycardia, and recently Wit and Cranefield¹⁶ showed that triggered tachycardias would also stop in response to premature stimulation. Massumi *et al.*¹⁷ first applied artificial pacing methods to the treatment of supraventricular tachycardia, and Durrer and colleagues¹⁸ confirmed these clinical results and stressed that the termination of tachycardia by premature beats required critical timing. When a single premature beat will suffice it may be simply provided by fixed rate underdrive pacing,¹¹ but if several depolarisations are required, overdrive pacing may be necessary. The termination of supraventricular tachycardia by overdrive atrial pacing was first reported in 1968¹⁹; by 1972, it was an accepted alternative to direct current cardioversion,²⁰ and it is now recognised as a very successful method for the termination of the majority of supraventricular tachycardias.²¹

Since the report by Haft *et al.* in 1967,¹ other investigators have confirmed that atrial flutter may be successfully converted to sinus rhythm by over-

drive atrial pacing, but there have been several dissenting reports. Puech *et al.*¹² succeeded in terminating immediately only six of 29 cases of atrial flutter and in 22 atrial fibrillation was the result. In six of these, however, the atrial fibrillation lasted only a few seconds. Rosen and colleagues¹³ treated 15 cases by overdrive atrial pacing: none reverted to sinus rhythm, but "stable" atrial fibrillation was induced in six patients. Our results were similarly poor before the administration of disopyramide. The poor results are probably a result of limiting the duration of pacing, the pacing rate, and the pacing energy. These limitations, which have not specifically been applied by others, were designed to minimise the risk of precipitating atrial fibrillation which did not occur in this series.

Disopyramide phosphate, a butyramide derivative, has been shown to reduce the frequency of automatically discharging foci and to slow the conduction velocity in both myocardial and specialised conduction tissue.²²⁻²³ In addition to its membrane stabilising effect disopyramide increases the duration of the action potential²³ and, in man, may prolong the atrial refractory period.²⁴⁻²⁵ Though the mechanism of atrial flutter is controversial,²⁶ some suggesting that abnormal automaticity²⁷⁻²⁸ is the cause and others preferring a re-entrant basis,²⁹⁻³¹ whichever the mechanism the electrophysiological properties of disopyramide could explain both the termination and the slowing of atrial flutter. If circus movement sustains the arrhythmia decreased atrial conduction velocity would lead to slowing of

the flutter rate but, if atrial refractoriness increased sufficiently to exceed the tachycardia cycle length, the arrhythmia would be extinguished. Alternatively, the depressant effect of disopyramide on spontaneous diastolic depolarisation would result in slowing, and possibly termination of atrial flutter caused by enhanced atrial automaticity. Decreased atrial excitability³² induced by disopyramide may also contribute to the termination of atrial flutter.

The effect of disopyramide on atrial flutter has not been reported in detail. Though Luoma *et al.*³³ studied patients with atrial flutter, they did not distinguish this arrhythmia from atrial fibrillation. In the cases reported by Vandenbosch *et al.*,³⁴ disopyramide converted three of 11 examples of atrial flutter and, in the series of Deano *et al.*,³⁵ three of eight patients reverted to sinus rhythm in response to disopyramide. Our rate of success with conversion was comparatively low and while this may be partly related to the short observation period, previous experience with intravenous disopyramide indicated that the majority of terminations occurred within 10 minutes of the start of the infusion³⁶ and, in any event, it is difficult to ascribe late terminations to the action of the drug.³⁷

In this series, as in others,³⁴⁻³⁵ disopyramide resulted in consistent and pronounced slowing of the atrial flutter frequency. In the presence of 1:1 atrioventricular conduction, the ventricular rate also slowed, but when a degree of atrioventricular conduction block was present, the infusion

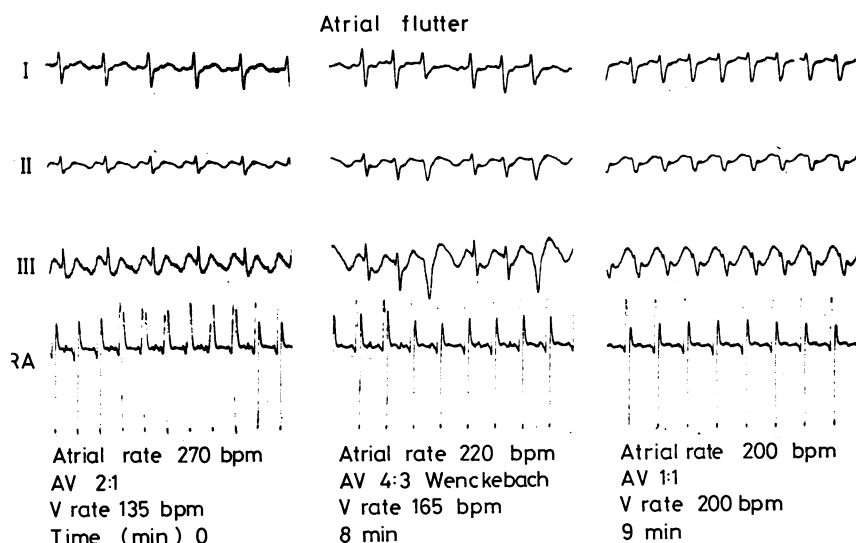


Fig. 5 Atrial flutter before (0) and 8 and 9 minutes after the infusion of disopyramide (case 7). See text for discussion. I, II, III are surface electrocardiogram leads. RA, right atrial electrogram. Paper speed, 25 mm/s.

of disopyramide resulted in higher ventricular rates in six cases. This result is a potential hazard when treating atrial flutter with disopyramide, and represents the combined effects of slowing of flutter frequency and anticholinergic effects on the atrio-

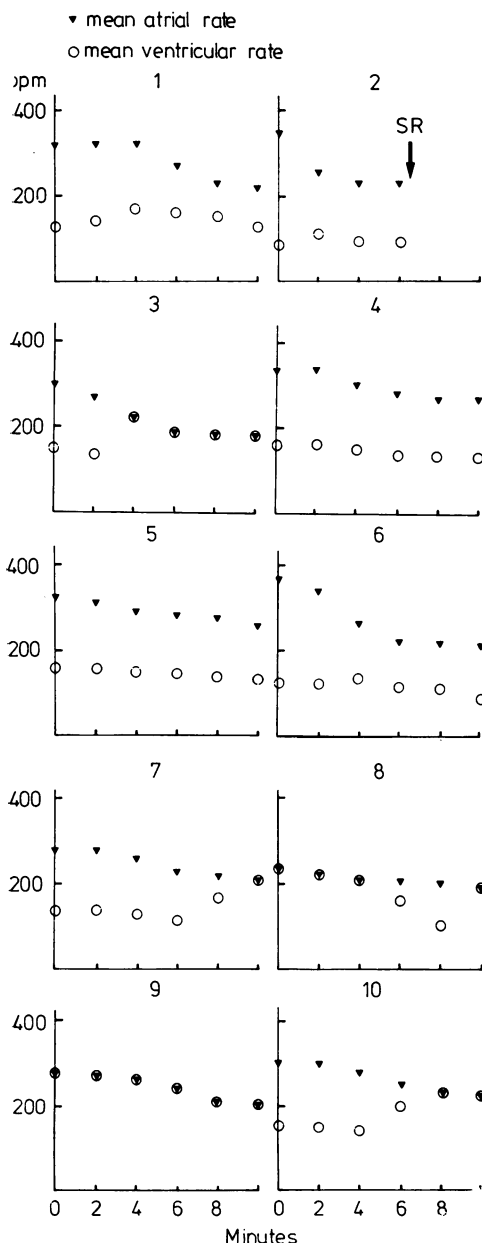


Fig. 6 Atrial and ventricular responses at 0, 2, 4, 6, 8, and 10 minutes, after disopyramide infusion in cases 1 to 10.

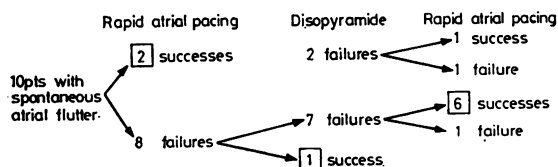


Fig. 7 Successful and unsuccessful conversion to sinus rhythm in 10 cases of atrial flutter.

ventricular node.^{25 38 39} When 1:1 atrioventricular conduction occurs after the treatment of atrial flutter with disopyramide the flutter frequency is considerably less than the pretreatment rate and very rapid ventricular rates do not result. Nevertheless, if disopyramide does not achieve conversion of atrial flutter to sinus rhythm the combination of increased ventricular rates and depressed myocardial function could lead to significant symptomatic deterioration and systemic hypotension. This serious side effect was not encountered in this study. Similar effects have been observed with quinidine⁴⁰⁻⁴² and procainamide.⁴³

The possibility that premedication with a quinidine-like antiarrhythmic agent would potentiate the conversion of atrial flutter to sinus rhythm by overdrive atrial pacing was suggested by Haft *et al.*¹ In one of their cases, rapid atrial pacing was effective only after administration of oral procainamide. In a recent report by Wyndham *et al.*⁴⁴ pre-treatment with disopyramide reduced the risk of atrial pacing precipitating atrial fibrillation and improved the chances of successful conversion of atrial flutter to sinus rhythm.

This study has attempted to assess systematically the value of premedication of atrial flutter with disopyramide before overdrive atrial pacing, and the results suggest that the conversion rate to sinus rhythm is improved. If atrial flutter were a result of circus movement, an increase of atrial refractoriness after disopyramide might increase the physiological obstacle around which the flutter wavelet circulated⁴⁵ allowing pacing closer to an enlarged circuit. Alternatively, if conduction slowed without a commensurate increase of refractoriness the excitable gap between the tachycardia depolarisation wavefront and its receding repolarised tail would increase. Either result would facilitate the invasion and "saturation" of the tachycardia circuit by pacemaker-induced depolarisation. On the other hand, if flutter were the result of abnormal automaticity, a disopyramide-induced reduction in the discharge rate would improve the electrophysiological access to the focus of the arrhythmia, unless disopyramide produced conspicuous increases in atrial refractoriness or conduction times.

Paroxysmal atrial flutter is difficult to treat effectively. Medical conversion of an individual paroxysm with drugs such as verapamil,⁴⁶ beta-blockers,⁴⁷ quinidine,⁴¹ and disopyramide,³⁴⁻³⁶ is generally disappointing and though synchronised direct current countershock is undoubtedly effective,⁴⁸ it is not without risk.⁴⁹⁻⁵⁰ A pacing method of terminating recurrent supraventricular arrhythmias has obvious attraction because it can be repeated often and may be adapted for long term use. Failure to achieve sinus rhythm and the unwanted precipitation of atrial fibrillation are the two main disadvantages of overdrive atrial pacing for the treatment of paroxysmal atrial flutter. Though the incidence of atrial fibrillation can be minimised by limiting the duration of pacing, the pacing frequency, and the pacing energy, the successful conversion rate of this arrhythmia to sinus rhythm is also reduced by these limitations. Premedication of atrial flutter with disopyramide restores the effectiveness of limited overdrive atrial pacing without increasing the risk of atrial fibrillation.

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